Helicterins A – F, Six New Dimeric (7.5′,8.2′)-Neolignans from the Indonesian Medicinal Plant *Helicteres isora*

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During a chemical study of Indonesian medicinal plants, we examined the constituents of fruits of *Helicteres isora* L. (Sterculiaceae), one of the famous Jamu medicines. From a H_2O extract of the fruits, we isolated six new neolignans, the helicterins A – F (**1** – **6**), and elucidated their structures by spectral analyses. Helicterins A – F (**1** – **6**) are dimeric (7.5′,8.2′)-neolignans with a bicyclo[2.2.2]octene C-framework, and showed mild inhibitory activity against reverse transcriptase from avian myeloblastosis virus.

1. Introduction. – *Helicteres isora* L. is a large arborescent shrub of the family Sterculiaceae, which grows in central and western India, southeast Asia, and the southern part of China. It is one of the best known articles of the Hindu Materia Medica and is used as one of Jamu medicines [1]. Timbers of this plant are used as an anthelmintic, and for colic and aphtha, while fruits are used for colic, as an anticonvulsant, and for abdominalgia [2]. Moreover, its pods are used as an antispasmodic, nervine tonic, antipyretic, antidiarrhoeal, antiparalytic, and antidysenteric in the traditional medicine of Saudi Arabia [3]. In addition, *Hattori* and co-workers reported an inhibitory activity of a H_2O extract of fruits of *H. isora* against reverse transcriptase from avian myeloblastosis virus (AMV-RT) [4] and anti-human immunodeficiency virus-type-1 (anti-HIV-1) activity [5]. Thus, we have examined constituents of the H_2O extract of fruits of *H. isora* and isolated two new (2.8′,5.7′)-neolignans[1]), named helisterculins A (**7**) and B (**8**), and a novel (2.8′,4.6′,5.7′)-neolignan, named helisorin (**9**) [9]. In this study, we have now isolated six new dimeric (2.8′,5,7′)-neolignans, named helicterins A – F (**1** – **6**), which showed inhibitory activity against AMV-RT. This paper

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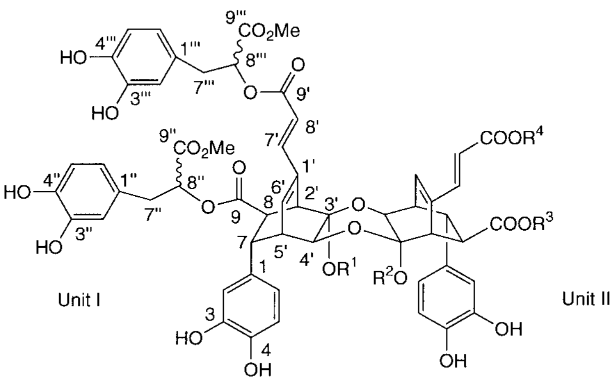
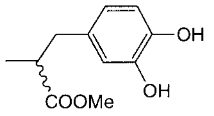
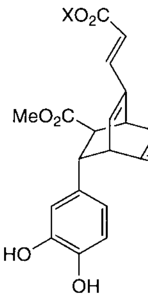
[1]) There are two definitions for 'lignan' and 'neolignan'. Based on structure, 'lignan' is defined as a compound composed of two C_6C_3 fragments linked β-β' (8-8′) [6] and 'neolignan' as a compound linked otherwise than β-β' [7]. Based on biosynthetic origin, on the other hand, 'neolignan' is defined as the product of oxidative coupling of allyl- or propenylphenols and 'lignan' as the coupling product of cinnamyl alcohols, *etc.* [8]. In this paper, the former definition is used because of its clarity.



	1	**2**	**3**	**4**	**5**	**6**
R^1	Me	H	Me	Me	H	Me
R^2	Me	Me	Me	Me	Me	H
R^3	X	X	Me	X	Me	X
R^4	X	X	X	Me	X	Me

X =





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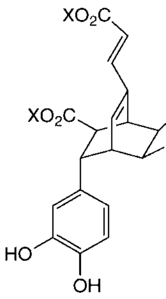

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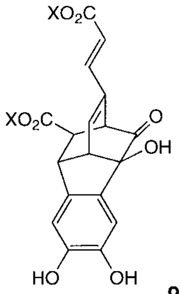

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reports their structure elucidation by spectroscopic means together with their AMV-RT inhibitory activities.

2. Structures of New Neolignans. – *Isolation.* Powdered dried fruits of *H. isora* were extracted with hot H_2O, and the extract was separated into AcOEt-soluble, BuOH-soluble, and H_2O-soluble fractions. Among them, the last one showing an inhibitory activity against AMV-RT was treated with the ion-exchange resin *Amberlite IR-120B* (H^+ form). Then, the MeOH-soluble portion of the H_2O eluate from the resin, which showed stronger AMV-RT inhibition, was further separated by a combination of *Diaion HP-20P*, *Sephadex LH-20*, and *MCI-gel CHP-20P* column chromatography (CC), prep. HPLC, and prep. TLC procedures to give helicterins A–F (**1**–**6**).

Helicterin A (**1**). The UV and IR spectra of the colorless amorphous solid **1** showed absorptions of phenyl (281 nm; 1630, 1521 cm^{-1}) and OH groups (3418 cm^{-1}) and of an ester CO group (1735 cm^{-1}), which were similar to those of helisterculin B (**8**) [9]. The ^1H- and ^{13}C-NMR spectra (*Tables 1* and *2*) were also very similar to those of **8** and

Table 1. *^{1}H-NMR Spectral Data for Neolignans* **1**–**6** *in CD_3OD*. Chemical shifts δ in ppm rel. to $SiMe_4$; coupling constants *J* in Hz. Arbitrary numbering[1]).

		1	**2**	**3**	**4**	**5**	**6**
Unit I	H–C(2)	6.82 (*d*, *J* = 2)	6.83 (*d*, *J* = 2)	6.82 (*d*, *J* = 2)	6.82 (*d*, *J* = 2)[a]	6.83 (*d*, *J* = 2)	6.87 (*d*, *J* = 2)
	H–C(5)	6.72 (*d*, *J* = 8)	6.71 (*d*, *J* = 8)	6.71 (*d*, *J* = 8)	6.70 (*d*, *J* = 8)[b]	6.705 (*d*, *J* = 8)	6.75 (*d*, *J* = 8)
	H–C(6)	6.62 (*dd*, *J* = 8, 2)	6.63 (*dd*, *J* = 8, 2)	6.62 (*dd*, *J* = 8, 2)	6.59 (*dd*, *J* = 8, 2)[c]	6.63 (*dd*, *J* = 8, 2)	6.68 (*dd*, *J* = 8, 2)
	H–C(7)	3.00 (*dd*, *J* = 6.5, 2.5)	2.990 (*dd*, *J* = 6.5, 3)	3.00 (*dd*, *J* = 6.5, 3)	2.97 (*dd*, *J* = 6.5, 2.5)[d]	2.98 (*dd*, *J* = 6.5, 3)	2.96 (*dd*, *J* = 6.5, 2.5)
	H–C(8)	3.08 (*dd*, *J* = 6.5, 1.5)	3.11 (*dd*, *J* = 6.5, 2)	3.07 (*dd*, *J* = 6.5, 2)	3.08 (*dd*, *J* = 6.5, 1.5)[e]	3.10 (*dd*, *J* = 6.5, 2)	3.48 (*dd*, *J* = 6.5, 2)
	H–C(2′)	3.59 (br. *s*)	3.59 (br. *s*)	3.59 (br. *s*)	*ca.* 3.59	3.58 (br. *s*)	3.29 (br. *s*)
	H–C(4′)	3.58 (*d*, *J* = 2.5)	3.83 (*d*, *J* = 3)	3.61 (*d*, *J* = 3)[a]	*ca.* 3.59	3.84 (*d*, *J* = 3)	3.60 (*d*, *J* = 2.5)
	H–C(5′)	2.73 (*dt*, *J* = 6.5, 2.5)	2.66 (*dt*, *J* = 6.5, 3)	2.73 (*dt*, *J* = 6.5, 3)[b]	2.74 (*dt*, *J* = 6.5, 2.5)	2.67 (*dt*, *J* = 6.5, 3)	2.74 (*dt*, *J* = 6.5, 2.5)
	H–C(6′)	6.34 (br. *d*, *J* = 6.5)	6.34 (br. *d*, *J* = 6.5)	6.36 (br. *d*, *J* = 6.5)	6.43 (br. *d*, *J* = 6.5)	6.36 (br. *d*, *J* = 6.5)	6.370 (br. *d*, *J* = 6.5)
	H–C(7′)	7.24 (*d*, *J* = 15.5)	7.26 (*d*, *J* = 15.5)	7.24 (*d*, *J* = 15.5)	7.24 (*d*, *J* = 15.5)	7.25 (*d*, *J* = 15.5)	7.23 (*d*, *J* = 15.5)
	H–C(8′)	5.92 (*d*, *J* = 15.5)	5.94 (*d*, *J* = 15.5)	5.92 (*d*, *J* = 15.5)	5.92 (*d*, *J* = 15.5)	5.92 (*d*, *J* = 15.5)	5.92 (*d*, *J* = 15.5)
	MeO–C(3′)	3.35 (*s*)	3.24 (*s*)	3.29 (*s*)[c]	3.25 (*s*)[f]	3.24 (*s*)	
	H–C(2″)	6.58 (*d*, *J* = 2)	6.59 (*d*, *J* = 2)	6.58 (*d*, *J* = 2)	6.57 (*d*, *J* = 2)[g]	6.58 (*d*, *J* = 2)	6.57 (*d*, *J* = 2)
	H–C(5″)	6.61 (*d*, *J* = 8)	6.62 (*d*, *J* = 8)	6.61 (*d*, *J* = 8)	6.620 (*d*, *J* = 8)[h]	6.62 (*d*, *J* = 8)	6.62 (*d*, *J* = 8)
	H–C(6″)	6.38 (*dd*, *J* = 8, 2)	6.39 (*dd*, *J* = 8, 2)	6.38 (*dd*, *J* = 8, 2)	6.38 (*dd*, *J* = 8, 2)[i]	6.39 (*dd*, *J* = 8, 2)	6.375 (*dd*, *J* = 8, 2)
	2 H–C(7″)	2.88 (*dd*, *J* = 14, 8.5)	2.81 (*dd*, *J* = 14.5, 8.5)	2.80 (*dd*, *J* = 14,8.5)	2.79 (*dd*, *J* = 14.5, 8.5)	2.80 (*dd*, *J* = 14.5, 8.5)	2.78 (*dd*, *J* = 14.5, 8)
		2.93 (*dd*, *J* = 14, 4.5)	2.93 (*dd*, *J* = 14.5, 5)	2.93 (*dd*, *J* = 14, 4.5)	2.93 (*dd*, *J* = 14.5, 5)	2.93 (*dd*, *J* = 14.5, 5)	2.88 (*dd*, *J* = 14.5, 4.5)
	H–C(8″)	4.97 (*dd*, *J* = 8.5, 4.5)	4.97 (*dd*, *J* = 8.5, 5)	4.97 (*dd*, *J* = 8.5, 4.5)	4.96 (*dd*, *J* = 8.5, 5)	4.96 (*dd*, *J* = 8.5, 5)	5.00 (*dd*, *J* = 8, 4.5)
	MeO–C(9″)	3.53 (*s*)	3.53 (*s*)[a]	3.74 (*s*)[d]	3.51 (*s*)[j]	3.53 (*s*)	3.53 (*s*)
	H–C(2‴)	6.71 (*d*, *J* = 2)	6.71 (*d*, *J* = 2)	6.70 (*d*, *J* = 2)	6.725 (*d*, *J* = 2)	6.710 (*d*, *J* = 2)	6.72 (*d*, *J* = 2)
	H–C(5‴)	6.68 (*d*, *J* = 8)	6.695 (*d*, *J* = 8)	6.68 (*d*, *J* = 8)	6.720 (*d*, *J* = 8)	6.69 (*d*, *J* = 8)	6.710 (*d*, *J* = 8)
	H–C(6‴)	6.60 (*dd*, *J* = 8, 2)	6.61 (*dd*, *J* = 8, 2)	6.60 (*dd*, *J* = 8, 2)[e]	6.61 (*dd*, *J* = 8, 2)	6.60 (*dd*, *J* = 8, 2)	6.60 (*dd*, *J* = 8, 2)
	2 H–C(7‴)	3.02 (*dd*, *J* = 15, 8.5)	3.03 (*dd*, *J* = 14.5, 8.5)	3.01 (*dd*, *J* = 14.5, 8.5)[f]	3.03 (*dd*, *J* = 14.5, 8.5)	3.03 (*dd*, *J* = 14.5, 8.5)[a]	3.04 (*dd*, *J* = 14.5, 8)
		3.11 (*dd*, *J* = 15, 4.5)	3.11 (*dd*, *J* = 14.5, 5)	3.11 (*dd*, *J* = 14.5, 4.5)	3.12 (*dd*, *J* = 14.5, 4.5)	3.11 (*dd*, *J* = 14.5, 4.5)	3.11 (*dd*, *J* = 14.5, 5)
	H–C(8‴)	5.28 (*dd*, *J* = 8.5, 4.5)	5.27 (*dd*, *J* = 8.5, 5)	5.28 (*dd*, *J* = 8.5, 4.5)[g]	5.26 (*dd*, *J* = 8.5, 4.5)	5.28 (*dd*, *J* = 8.5, 4.5)[b]	5.24 (*dd*, *J* = 8, 5)
	MeO–C(9‴)	3.72 (*s*)	3.72 (*s*)[b]	3.73 (*s*)[d]	3.74 (*s*)	3.75 (*s*)[c]	3.73 (*s*)
Unit II	H–C(2)	6.82 (*d*, *J* = 2)	6.89 (*d*, *J* = 2)	6.86 (*d*, *J* = 2)	6.84 (*d*, *J* = 2)[a]	6.89 (*d*, *J* = 2)	6.84 (*d*, *J* = 2)
	H–C(5)	6.72 (*d*, *J* = 8)	6.74 (*d*, *J* = 8)	*ca.* 6.705	6.730 (*d*, *J* = 8)[b]	6.725 (*d*, *J* = 8)	6.715 (*d*, *J* = 8)
	H–C(6)	6.62 (*dd*, *J* = 8, 2)	6.690 (*dd*, *J* = 8, 2)	*ca.* 6.705	6.630 (*dd*, *J* = 8, 2)[c]	6.76 (*dd*, *J* = 8, 2)	6.64 (*dd*, *J* = 8, 2)
	H–C(7)	3.00 (*dd*, *J* = 6.5, 2.5)	2.995 (*dd*, *J* = 6.5, 3)	*ca.* 3.12	2.99 (*dd*, *J* = 6.5, 2.5)[d]	3.12 (*dd*, *J* = 6.5, 3)	2.97 (*dd*, *J* = 7, 2.5)
	H–C(8)	3.08 (*dd*, *J* = 6.5, 1.5)	3.49 (*dd*, *J* = 6.5, 2)	*ca.* 3.12	3.12 (*dd*, *J* = 6.5, 1.5)[e]	3.44 (*dd*, *J* = 6.5, 2)	3.15 (*dd*, *J* = 7, 1.5)
	MeO–C(9)			3.53 (*s*)		3.51 (*s*)	
	H–C(2′)	3.59 (br. *s*)	3.28 (br. *s*)	3.60 (br. *s*)	*ca.* 3.59	3.31 (br. *s*)	3.60 (br. *s*)
	H–C(4′)	3.58 (*d*, *J* = 2.5)	3.58 (*d*, *J* = 3)	3.60 (*d*, *J* = 3)[a]	*ca.* 3.59	3.60 (*d*, *J* = 3)	3.84 (*d*, *J* = 2.5)
	H–C(5′)	2.73 (*dt*, *J* = 6.5, 2.5)	2.74 (*dt*, *J* = 6.5, 3)	2.74 (*dt*, *J* = 6.5, 3)[b]	2.74 (*dt*, *J* = 6.5, 2.5)	2.74 (*dt*, *J* = 6.5, 3)	2.67 (*dt*, *J* = 6.5, 2.5)
	H–C(6′)	6.34 (br. *d*, *J* = 6.5)	6.29 (br. *d*, *J* = 6.5)	6.34 (br. *d*, *J* = 6.5)	6.35 (br. *d*, *J* = 6.5)	6.30 (br. *d*, *J* = 6.5)	6.34 (br. *d*, *J* = 6.5)
	H–C(7′)	7.24 (*d*, *J* = 15.5)	7.25 (*d*, *J* = 15.5)	7.26 (*d*, *J* = 15.5)	7.22 (*d*, *J* = 15.5)	7.26 (*d*, *J* = 15.5)	7.23 (*d*, *J* = 15.5)
	H–C(8′)	5.92 (*d*, *J* = 15.5)	5.93 (*d*, *J* = 15.5)	5.87 (*d*, *J* = 15.5)	5.89 (*d*, *J* = 15.5)	5.86 (*d*, *J* = 15.5)	5.89 (*d*, *J* = 15.5)
	MeO–C(3′)	3.35 (*s*)		3.22 (*s*)[c]	3.23 (*s*)[f]		3.27 (*s*)
	MeO–C(9′)				3.77 (*s*)		3.78 (*s*)
	H–C(2″)	6.58 (*d*, *J* = 2)	6.54 (*d*, *J* = 2)		6.58 (*d*, *J* = 2)[g]		6.54 (*d*, *J* = 2)
	H–C(5″)	6.61 (*d*, *J* = 8)	6.60 (*d*, *J* = 8)		6.6625 (*d*, *J* = 8)[h]		6.60 (*d*, *J* = 8)
	H–C(6″)	6.38 (*dd*, *J* = 8, 2)	6.33 (*dd*, *J* = 8, 2)		6.39 (*dd*, *J* = 8, 2)[i]		6.32 (*dd*, *J* = 8, 2)
	2 H–C(7″)	2.88 (*dd*, *J* = 14, 8.5)	2.80 (*dd*, *J* = 14.5, 8.5)		2.85 (*dd*, *J* = 14, 7.5)		2.85 (*dd*, *J* = 14, 8)
		2.93 (*dd*, *J* = 14, 4.5)	2.89 (*dd*, *J* = 14.5, 5)		2.94 (*dd*, *J* = 14, 5)		2.94 (*dd*, *J* = 14, 4.5)
	H–C(8″)	4.97 (*dd*, *J* = 8.5, 4.5)	4.99 (*dd*, *J* = 8.5, 5)		5.01 (*dd*, *J* = 7.5, 5)		4.97 (*dd*, *J* = 8, 4.5)
	MeO–C(9″)	3.53 *s*	3.54 (*s*)[a]		3.60 (*s*)[j]		3.60 (*s*)
	H–C(2‴)	6.71 (*d*, *J* = 2)	6.71 (*d*, *J* = 2)	6.70 (*d*, *J* = 2)		6.720 (*d*, *J* = 2)	
	H–C(5‴)	6.68 (*d*, *J* = 8)	6.700 (*d*, *J* = 8)	6.69 (*d*, *J* = 8)		6.70 (*d*, *J* = 8)	
	H–C(6‴)	6.60 (*dd*, *J* = 8, 2)	6.61 (*dd*, *J* = 8, 2)	6.59 (*dd*, *J* = 8, 2)[e]		6.59 (*dd*, *J* = 8, 2)	
	2 H–C(7‴)	3.02 (*dd*, *J* = 15, 8.5)	3.03 (*dd*, *J* = 14.5, 8.5)	3.02 (*dd*, *J* = 14.5, 8.5)[f]		3.01 (*dd*, *J* = 14.5, 8.5)[a]	
		3.11 (*dd*, *J* = 15, 4.5)	3.09 (*dd*, *J* = 14.5, 5)	3.11 (*dd*, *J* = 14.5, 4.5)		3.11 (*dd*, *J* = 14.5, 4.5)	
	H–C(8‴)	5.28 (*dd*, *J* = 8.5, 4.5)	5.28 (*dd*, *J* = 8.5, 5)	5.27 (*dd*, *J* = 8.5, 4.5)[f]		5.26 (*dd*, *J* = 8.5, 4.5)[b]	
	MeO–C(9‴)	3.72 (*s*)	3.71 (*s*)[b]	3.53 (*s*)		3.74 (*s*)[c]	

[a]–[j] Assignments may be interchanged.

Table 2. *^{13}C-NMR Spectral Data for Neolignans* **1**–**6** *in CD_3OD.* δ in ppm relative to $SiMe_4$. Arbitrary numbering1)).

	1		**2**		**3**		**4**		**5**		**6**	
	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II	Unit I	Unit II
C(1)	134.2	134.2	134.3	134.4	134.3a)	134.2a)	134.1a)	134.2a)	134.3	134.4	134.3	134.3
C(2)	117.2	117.2	117.2a)	117.4a)	117.2	117.4	117.2b)	117.2b)	117.2	117.6	117.4	117.2
C(3)	146.9	146.9	146.9b)	146.9b)	146.9	146.9	146.9c)	146.9c)	146.7a)	146.7a)	146.7a)	146.8a)
C(4)	145.8	145.8	145.98c)	145.7c)	145.9	145.9	145.8d)	145.8d)	145.7b)	145.7b)	145.7b)	145.7b)
C(5)	117.1	117.1	117.2a)	117.2a)	117.1	117.2	117.1b)	117.2b)	117.2	117.1	117.2	117.2
C(6)	121.5	121.5	121.7	121.7	121.6	121.6	121.5	121.5	121.6	121.6	121.7	121.7
C(7)	44.9	44.9	45.1	45.5	45.0	45.0	45.0e)	45.1e)	45.1	45.2	45.6	45.2
C(8)	44.0	44.0	43.8	44.8	44.1	44.3	44.0	44.0	43.8	44.9	44.8	43.9
C(9)	175.2	175.2	175.3	175.8	175.2	176.4	175.2	175.2	175.4	176.9	175.8	175.3
MeO–C(9)										53.4		
C(1′)	137.8	137.8	137.8	139.3	137.9	137.7	138.0	137.8	137.8	139.0	139.4	137.8
C(2′)	42.0	42.0	42.0	47.9	42.0	42.3	41.9	41.9	42.0	48.2	47.9	41.9
C(3′)	102.2	102.2	102.4	98.8	102.3b)	102.1b)	102.26f)	102.32f)	102.4	98.7	98.8	102.4
C(4′)	71.4	71.4	71.0	70.8	71.4c)	71.5c	71.4	65.0	71.1	70.7	70.8	71.0
C(5′)	46.5	46.5	46.9	46.8	46.5d)	46.7d)	46.5g)	46.4g)	46.9	47.1	46.8	46.8
C(6′)	142.9	142.9	143.2	141.7	142.8	143.4	142.7	142.3	143.2	142.4	141.5	142.6
C(7′)	146.3	146.3	146.5	146.7	146.4	146.6	146.2	145.4	146.5	146.9	146.6	145.6
C(8′)	117.5	117.5	117.3a)	117.3a)	117.6	116.9	117.6	118.2	117.3	116.8	117.3	118.05
C(9′)	169.2	169.2	169.3	169.3	169.2	169.0	169.2	170.7	169.2c)	169.3c)	169.3	170.8
MeO–C(3′)	50.7	50.7	50.0	50.0	49.9	49.9	50.0	50.0	50.2	50.2		
MeO–C(9′)								53.0				53.0
C(1″)	129.3	129.3	129.3	129.2	129.3		129.3	129.1	129.3		129.2	129.1
C(2″)	118.2	118.2	118.2	118.0	118.2		118.2	118.2	118.2		118.2	118.11
C(3″)	146.9	146.9	146.9b)	146.9b)	146.9		146.9c)	146.9c)	146.9a)		146.8a)	146.8a)
C(4″)	145.9	145.9	146.04c)	146.04c)	146.1		146.0d)	146.0d)	145.7b)		145.9b)	146.0b)
C(5″)	117.1	117.1	117.2a)	117.1a)	117.2		117.2b)	117.2b)	117.2		117.1	117.2
C(6″)	122.6	122.6	122.6	122.7	122.6		122.57h)	122.57h)	122.6		122.6	122.7
C(7″)	38.4	38.4	38.4	38.4	38.4		38.4	38.4	38.4	38.42	38.36	
C(8″)	75.6	75.6	75.6	75.7	75.6		75.6	75.5	75.6		75.5	75.7
C(9″)	172.1	172.1	172.2	172.2	172.2		172.2	172.2	172.3		172.3	172.2
MeO–C(9″)	53.5	53.5	53.5	53.5	53.4		53.5i)	53.4i)	53.6		53.53	53.47
C(1‴)	129.6	129.6	129.6	129.6	129.6	129.6	129.6		129.6		129.6	
C(2‴)	117.8	117.8	117.92d)	117.86d)	117.9	118.0	117.9		118.0	117.9	117.99	
C(3‴)	147.0	147.0	147.0b)	147.0b)	147.1	147.1	147.0c)		147.0a)	147.0a)	147.0a)	
C(4‴)	146.0	146.0	146.04c)	145.98c)	146.1	146.1	146.0d)		146.0b)	146.0b)	146.0b)	
C(5‴)	117.2	117.2	117.2a)	117.2a)	117.2	117.2	117.2b)		117.2	117.2	117.2	
C(6‴)	122.6	122.6	122.6	122.6	122.5	122.5	122.57h)		122.5	122.5	122.6	
C(7‴)	38.5	38.5	38.5	38.5	38.5	38.5	38.5		38.5	38.5	38.6	
C(8‴)	75.3	75.3	75.3	75.4	75.3	75.3	75.4		75.3	75.3	75.4	
C(9‴)	172.9	172.9	173.0	173.0	173.0	173.0	173.0		173.0	173.0	173.0	
MeO–C(9‴)	53.6	53.6	53.6	53.6	53.6e)	53.5e)	53.6		53.7	53.7	53.7	

a)–i)) Assignments may be interchanged in each compound.

revealed signals due to three sets of 1,3,4-trisubstituted benzene rings, two (a *trans*-disubstituted and a trisubstituted) olefins moieties and seven methine (including three O-substituted ones), two methylene, and four ester CO groups. But they were also characterized by the presence of signals of an additional MeO group and a ketal C-atom and the lack of a signal of a ketone CO C-atom. These spectral data suggested that **1** could be a compound having a ketal group instead of the ketone group present in helisorin (**9**). However, the negative-ion FAB-MS of **1** showed the *quasi*-molecular ion peak at *m/z* 1523, almost double of that of **8** ($C_{38}H_{38}O_{16}$, M_r 751), and its molecular formula was determined to be $C_{78}H_{76}O_{32}$ by high-resolution FAB-MS. Thus, helicterin A (**1**) was considered a dimeric neolignan having a symmetric structure. The planar structure of the monomer unit of **1** was determined by analyses of the COSY, HETCOR, and HMBC data (*Table 3*) and the relative configuration at the bicyclic moiety of **1** by a series of NOE experiments.

Three 3,4-dihydroxyphenyl moieties of **1** (C(1) to C(6), C(1″) to C(6″), C(1‴) to C(6‴)) were each connected to a benzylic C-atom (C(7), C(7″), and C(7‴), resp.), as shown by the long-range correlations between the benzylic proton(s) or C-atoms and the corresponding C-atom or proton(s), respectively (H−C(7)/C(2), C(6); H−C(7″)/C(2″), C(6″); H−C(7‴)/C(2‴), C(6‴); C(7)/H−C(2), H−C(6); C(7″)/H−C(2″), H−C(6″); C(7‴)/H−C(2‴), H−C(6‴)) (arbitrary numbering, see *Formula 1*). Likewise, the structures of the ester moieties were deduced from the three-bond correlations of the carbonyl C-atoms (C(9)/H−C(7), H−C(2′), H−C(8″); C(9′)/H−C(7′), H−C(8‴); C(9″)/H−C(7″), MeO−C(9″); C(9‴)/H−C(7‴), MeO−C(9‴)). Furthermore, the ketal C-atom was assigned as C(3′) and was determined to carry a MeO group, based on the long-range correlations with H−C(8), H−C(2′), H−C(4′), and MeO−C(3′).

In CD_3OD, NOE enhancements were observed from H−C(2) to H−C(7) and H−C(8), from H−C(6) to H−C(7), and from MeO−C(3′) to H−C(2), H−C(6), and H−C(8), indicating the configuration at C(7), C(8), and C(3′). In (D_6)acetone, which gives a good separation of the H−C(2′) and H−C(4′) signals, NOE enhancements were observed from H−C(4′) to H−C(2) and H−C(6), confirming the configuration at C(4′).

As mentioned above, helicterin A (**1**) was considered to be a dimeric neolignan having a symmetric structure, and thus, two types of connectivity of the monomer units could be possible, one having the C(I-3′)−C(II-4′) and C(I-4′)−C(II-3′) connectivities (type **A** in the *Fig.*) and the other having the C(I-3′)−C(II-3′) and C(I-4′)−C(II-4′) connectivities (type **B** in the *Fig.*). Although we could not obtain positive evidence on **1**, a structure of type **A** was concluded for **1** from the spectral comparison with the nonsymmetrical compound helicterin B (**2**) (*vide infra*).

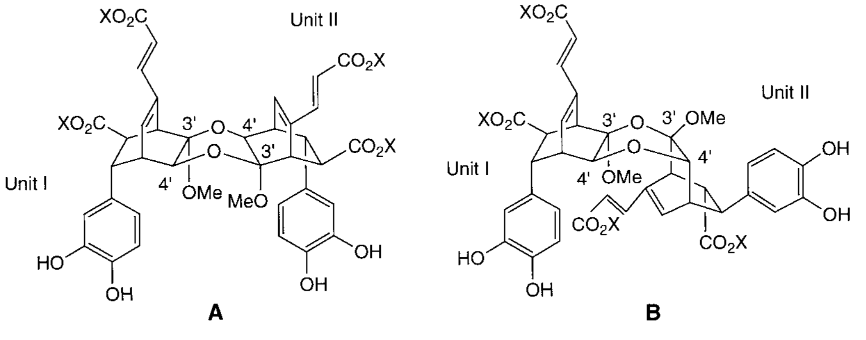

Figure. *Probable connectivities of two monomer units for symmetrical structure of helicterin A* (**1**)

Helicterin B (**2**). The colorless amorphous solid **2** had the molecular formula $C_{77}H_{74}O_{32}$, corresponding to one fewer methylene group than in **1**. The UV and IR spectra were similar to those of **1**, suggesting the presence of phenyl, OH, and ester CO groups. The ^{1}H- and ^{13}C-NMR spectra of **2** (*Tables 1* and *2*) also resembled those of **1**,

Table 3. *Long-Range Correlated Protons in the HMBC Spectra of Neolignans* **1**–**6** *in CD_3OD.* Arbitrary numbering[1]).

		1	**2**	**3**	**4**	**5**	**6**
Unit I	C(1)	H–C(5), H–C(7), H–C(8)	H–C(5), H–C(7), H–C(8)	H–C(5), H–C(7), H–C(8)	H–C(5), H–C(7), H–C(8)	H–C(5), H–C(7), H–C(8)	H–C(5), H–C(7), H–C(8)
	C(2)	H–C(6), H–C(7)	H–C(6), H–C(7)	H–C(6), H–C(7)	H–C(6), H–C(7)	H–C(6), H–C(7)	H–C(6), H–C(7)
	C(3)	H–C(2), H–C(5)	H–C(2), H–C(5)	H–C(2), H–C(5)	H–C(2), H–C(5)	H–C(2), H–C(5)	H–C(2), H–C(5)
	C(4)	H–C(2), H–C(5), H–C(6)	H–C(2), H–C(5), H–C(6)	H–C(2), H–C(6)	H–C(2), H–C(6)	H–C(2), H–C(6)	H–C(2), H–C(6)
	C(6)	H–C(2), H–C(7)	H–C(2), H–C(7)	H–C(2), H–C(7)	H–C(2), H–C(7)	H–C(2), H–C(7)	H–C(2), H–C(7)
	C(7)	H–C(2), H–C(6), H–C(8), H–C(2′), H–C(4′)	H–C(2), H–C(8), H–C(2′)	H–C(2), H–C(6), H–C(8), H–C(4′)	H–C(2), H–C(6), H–C(8), H–C(4′)	H–C(2), H–C(6), H–C(8)	H–C(2), H–C(6)
	C(8)	H–C(7)	H–C(7), H–C(5′)	H–C(7)	H–C(7), H–C(5′)		H–C(2′), H–C(5′)
	C(9)	H–C(7), H–C(8), H–C(2′), H–C(8″)	H–C(7), H–C(8), H–C(8″)	H–C(7), H–C(8), H–C(8″)	H–C(7), H–C(8), H–C(8″)	H–C(7), H–C(8),	H–C(7), H–C(8), H–C(8″)
	C(1′)	H–C(8), H–C(2′), H–C(5′), H–C(7′), H–C(8′)	H–C(8), H–C(2′), H–C(5′), H–C(7′), H–C(8′)	H–C(8), H–C(2′), H–C(5′), H–C(7′), H–C(8′)	H–C(8), H–C(2′), H–C(5′), H–C(7′), H–C(8′)	H–C(8), H–C(5′), H–C(7′), H–C(8′)	H–C(8), H–C(5′) H–C(7′), H–C(8′)
	C(2′)	H–C(8), H–C(6′), H–C(7′)	H–C(8), H–C(6′), H–C(7′)	H–C(7), H–C(6′), H–C(7′)	H–C(8), H–C(6′), H–C(7′)		H–C(8), H–C(6′), H–C(7′)
	C(3′)	H–C(8), H–C(2′), H–C(4′), MeO–C(3′)	H–C(8), H–C(2′), H–C(4′), H–C(5′), MeO–C(3′), H–C(II-4′)	H–C(8), H–C(2′), H–C(4′), H–C(5′), MeO–C(3′), H–C(II-4′)	H–C(7), H–C(2′), H–C(4′), H–C(5′), MeO–C(3′), H–C(II-4′)	H–C(2′), MeO–C(3′)	H–C(8), H–C(2′), H–C(5′)
	C(4′)	H–C(7), H–C(2′)	H–C(7), H–C(2′)	H–C(7)	H–C(2′)		H–C(7)
	C(5′)	H–C(4′), H–C(6′)	H–C(7), H–C(6′)	H–C(6′)	H–C(7), H–C(6′)		H–C(7), H–C(6′)
	C(6′)	H–C(2′), H–C(4′), H–C(7′)	H–C(2′), H–C(4′), H–C(7′)	H–C(2′), H–C(4′), H–C(7′)	H–C(2′), H–C(4′), H–C(7′)	H–C(7′)	H–C(7′)
	C(7′)	H–C(6′)		H–C(6′)	H–C(6′)	H–C(6′)	
	C(8′)	H–C(7′)	H–C(7′)	H–C(7′)	H–C(7′)		
	C(9′)	H–C(7′), H–C(8′), H–C(8‴)	H–C(7′), H–C(8′), H–C(8‴)	H–C(7′), H–C(8′), H–C(8‴)	H–C(7′), H–C(8′), MeO–C(9′)	H–C(7′), H–C(8′), H–C(8‴)	H–C(7′), H–C(8′), H–C(8‴)
	C(1″)	H–C(5″), H–C(7″), H–C(8″)	H–C(5″), H–C(7″), H–C(8″)	H–C(5″), H–C(7″),	H–C(5″), H–C(7″), H–C(8″)	H–C(5″), H–C(7″), H–C(8″)	H–C(5″), H–C(7″), H–C(8″)
	C(2″)	H–C(6″), H–C(7″)	H–C(6″), H–C(7″)	H–C(6″), H–C(7″)	H–C(6″), H–C(7″)	H–C(6″), H–C(7″)	H–C(6″), H–C(7″)
	C(3″)	H–C(2″), H–C(5″)	H–C(2″), H–C(5″)	H–C(2″), H–C(5″)	H–C(2″), H–C(5″)	H–C(2″), H–C(5″)	H–C(2″), H–C(5″)
	C(4″)	H–C(2″), H–C(5″), H–C(6″)	H–C(2″), H–C(5″), H–C(6″)	H–C(2″), H–C(6″)	H–C(2″), H–C(6″)	H–C(2″), H–C(6″)	H–C(2″), H–C(6″)
	C(6″)	H–C(2″), H–C(7″)	H–C(2″), H–C(7″)	H–C(2″), H–C(7″)	H–C(2″), H–C(7″)	H–C(2″), H–C(7″)	H–C(2″), H–C(7″)
	C(7″)	H–C(2″), H–C(6″), H–C(8″)	H–C(2″), H–C(6″), H–C(8″)		H–C(2″), H–C(6″), H–C(8″)		H–C(6″), H–C(8″)
	C(8″)	H–C(7″)	H–C(7″)	H–C(7″)	H–C(7″)	H–C(7″)	H–C(7″)
	C(9″)	H–C(7″), H–C(8″), MeO–C(9″)	H–C(7″), H–C(8″), MeO–C(9″)	H–C(7″), H–C(8″), MeO–C(9″)	H–C(7″), H–C(8″), MeO–C(9″)	H–C(7″), H–C(8″), MeO–C(9″)	H–C(7″), H–C(8″), MeO–C(9″)
	C(1‴)	H–C(5‴), H–C(7‴), H–C(8‴)	H–C(5‴), H–C(7‴), H–C(8‴)	H–C(5‴), H–C(7‴), H–C(8‴)	H–C(5‴), H–C(7‴), H–C(8‴)	H–C(5‴), H–C(7‴), H–C(8‴)	H–C(5‴), H–C(7‴), H–C(8‴)
	C(2‴)	H–C(6‴), H–C(7‴)	H–C(6‴), H–C(7‴)	H–C(6‴), H–C(7‴)	H–C(6‴), H–C(7‴)	H–C(6‴), H–C(7‴)	H–C(6‴), H–C(7‴)
	C(3‴)	H–C(2‴), H–C(5‴)	H–C(2‴), H–C(5‴)	H–C(2‴), H–C(5‴)	H–C(2‴), H–C(5‴)	H–C(2‴), H–C(5‴)	H–C(2‴), H–C(5‴)
	C(4‴)	H–C(2‴), H–C(5‴), H–C(6‴)	H–C(2‴), H–C(5‴), H–C(6‴)	H–C(2‴), H–C(6‴)	H–C(2‴), H–C(5‴), H–C(6‴)	H–C(2‴), H–C(6‴)	H–C(2‴), H–C(6‴)
	C(6‴)	H–C(2‴), H–C(7‴)	H–C(2‴), H–C(7‴)	H–C(2‴), H–C(7‴)	H–C(2‴), H–C(7‴)	H–C(2‴), H–C(7‴)	H–C(2‴), H–C(7‴)
	C(7‴)	H–C(2‴), H–C(6‴), H–C(8‴)	H–C(2‴), H–C(6‴), H–C(8‴)	H–C(2‴), H–C(6‴), H–C(8‴)	H–C(2‴), H–C(6‴), H–C(8‴)	H–C(2‴), H–C(8‴)	H–C(6‴), H–C(8‴)
	C(8‴)	H–C(7‴)	H–C(7‴)	H–C(7‴)	H–C(7‴)	H–C(7‴)	H–C(7‴)
	C(9‴)	H–C(7‴), H–C(8‴), MeO–C(9‴)	H–C(7‴), H–C(8‴), MeO–C(9‴)	H–C(7‴), H–C(8‴), MeO–C(9‴)	H–C(7‴), H–C(8‴), MeO–C(9‴)	H–C(7‴), H–C(8‴), MeO–C(9‴)	H–C(7‴), H–C(8‴), MeO–C(9‴)

Table 3 (cont.)

		1	**2**	**3**	**4**	**5**	**6**
Unit II	C(1)	H−C(5), H−C(7), H−C(8)	H−C(5), H−C(7), H−C(8)	H−C(5), H−C(7), H−C(8)	H−C(5), H−C(7), H−C(8)	H−C(5), H−C(7), H−C(8)	H−C(5), H−C(8)
	C(2)	H−C(6), H−C(7)	H−C(6), H−C(7)	H−C(6), H−C(7)	H−C(6), H−C(7)	H−C(6), H−C(7)	H−C(6), H−C(7)
	C(3)	H−C(2), H−C(5)	H−C(2), H−C(5)	H−C(2), H−C(5)	H−C(2), H−C(5)	H−C(2), H−C(5)	H−C(2), H−C(5)
	C(4)	H−C(2), H−C(5), H−C(6)	H−C(2), H−C(5), H−C(6)	H−C(2), H−C(6)	H−C(2), H−C(6)	H−C(2), H−C(6)	H−C(2), H−C(6)
	C(6)	H−C(2), H−C(7)	H−C(2), H−C(7)	H−C(2), H−C(7)	H−C(2), H−C(7)	H−C(2), H−C(7)	H−C(2), H−C(7)
	C(7)	H−C(2), H−C(6), H−C(8), H−C(2′), H−C(4′)	H−C(2), H−C(8), H−C(2′)	H−C(2), H−C(6), H−C(8), H−C(4′)	H−C(2), H−C(6), H−C(8), H−C(4′)	H−C(2), H−C(6)	H−C(2), H−C(6)
	C(8)	H−C(7)	H−C(7), H−C(5′)	H−C(7)	H−C(7), H−C(5′)		H−C(7)
	C(9)	H−C(7), H−C(8), H−C(2′), H−C(8″)	H−C(7), H−C(8), H−C(8″)	H−C(7), H−C(8), MeO−C(9)	H−C(7), H−C(8), H−C(8″)	H−C(8), MeO−C(9)	H−C(7), H−C(8)
	C(1′)	H−C(8), H−C(2′), H−C(5′), H−C(7′), H−C(8′)	H−C(8), H−C(5′), H−C(7′), H−C(8′)	H−C(8), H−C(2′), H−C(5′), H−C(7′), H−C(8′)	H−C(8), H−C(2′), H−C(5′), H−C(7′), H−C(8′)	H−C(8), H−C(5′), H−C(7′), H−C(8′)	H−C(8), H−C(5′), H−C(7′), H−C(8′)
	C(2′)	H−C(8), H−C(6′), H−C(7′)	H−C(8), H−C(6′), H−C(7′)	H−C(7), H−C(6′), H−C(7′)	H−C(8), H−C(6′), H−C(7′),	H−C(7), H−C(8)	H−C(8), H−C(6′), H−C(7′),
	C(3′)	H−C(8), H−C(2′), H−C(4′), MeO−C(3′)	H−C(8), H−C(2′), H−C(5′), H−C(II-4′)	H−C(8), H−C(2′), H−C(4′), H−C(5′), MeO−C(3′), H−C(II-4′)	H−C(7), H−C(2′), H−C(4′), H−C(5′), MeO−C(3′), H−C(II-4′)		H−C(8), H−C(2′), H−C(5′), MeO−C(3′), H−C(II-4′)
	C(4′)	H−C(7), H−C(2′)	H−C(7)	H−C(7)	H−C(2′)		H−C(7)
	C(5′)	H−C(4′), H−C(6′)	H−C(6′), H−C(7)	H−C(6′)	H−C(7), H−C(6′)		H−C(7), H−C(6′)
	C(6′)	H−C(2′), H−C(4′), H−C(7′)	H−C(4′), H−C(7′)	H−C(2′), H−C(4′), H−C(7′)	H−C(2′), H−C(4′), H−C(7′)	H−C(7′)	H−C(7′)
	C(7′)	H−C(6′)		H−C(6′)	H−C(6′)	H−C(6′)	
	C(8′)	H−C(7′)	H−C(7′)	H−C(7′)	H−C(7′)		
	C(9′)	H−C(7′), H−C(8′), H−C(8‴)	H−C(7′), H−C(8′), H−C(8‴)	H−C(7′), H−C(8′), H−C(8‴)	H−C(7′), H−C(8′), MeO−C(9′)	H−C(7′), H−C(8′), H−C(8‴)	H−C(7′), H−C(8′), MeO−C(9′)
	C(1″)	H−C(5″), H−C(7″), H−C(8″)	H−C(5″), H−C(7″), H−C(8″)		H−C(5″), H−C(7″), H−C(8″)		H−C(5″), H−C(7″), H−C(8″)
	C(2″)	H−C(6″), H−C(7″)	H−C(6″), H−C(7″)		H−C(6″), H−C(7″)		H−C(6″), H−C(7″)
	C(3″)	H−C(2″), H−C(5″)	H−C(2″), H−C(5″)		H−C(2″), H−C(5″)		H−C(2″), H−C(5″)
	C(4″)	H−C(2″), H−C(5″), H−C(6″)	H−C(2″), H−C(5″), H−C(6″)		H−C(2″), H−C(6″)		H−C(2″), H−C(6″)
	C(6″)	H−C(2″), H−C(7″)	H−C(2″), H−C(7″)		H−C(2″), H−C(7″)		H−C(2″), H−C(7″)
	C(7″)	H−C(2″), H−C(6″), H−C(8″)	H−C(2″), H−C(6″), H−C(8″)		H−C(2″), H−C(6″), H−C(8″)		H−C(6″), H−C(8″)
	C(8″)	H−C(7″)	H−C(7″)		H−C(7″)		H−C(7″)
	C(9″)	H−C(7″), H−C(8″), MeO−C(9″)	H−C(7″), H−C(8″), MeO−C(9″)		H−C(7″), H−C(8″), MeO−C(9″)		H−C(7″), H−C(8″), MeO−C(9″)
	C(1‴)	H−C(5‴), H−C(7‴), H−C(8‴)	H−C(5‴), H−C(7‴), H−C(8‴)	H−C(5‴), H−C(7‴), H−C(8‴)		H−C(5‴), H−C(7‴), H−C(8‴)	
	C(2‴)	H−C(6‴), H−C(7‴)	H−C(6‴), H−C(7‴)	H−C(6‴), H−C(7‴)		H−C(6‴), H−C(7‴)	
	C(3‴)	H−C(2‴), H−C(5‴)	H−C(2‴), H−C(5‴)	H−C(2‴), H−C(5‴)		H−C(2‴), H−C(5‴)	
	C(4‴)	H−C(2‴), H−C(5‴), H−C(6‴)	H−C(2‴), H−C(5‴), H−C(6‴)	H−C(2‴), H−C(6‴)		H−C(2‴), H−C(6‴)	
	C(6‴)	H−C(2‴), H−C(7‴)	H−C(2‴), H−C(7‴)	H−C(2‴), H−C(7‴)		H−C(2‴), H−C(7‴)	
	C(7‴)	H−C(2‴), H−C(6‴), H−C(8‴)	H−C(2‴), H−C(6‴), H−C(8‴)	H−C(2‴), H−C(6‴), H−C(8‴)		H−C(2‴), H−C(8‴)	
	C(8‴)	H−C(7‴)	H−C(7‴)	H−C(7‴)		H−C(7‴)	
	C(9‴)	H−C(7‴), H−C(8‴), MeO−C(9‴)	H−C(7‴), H−C(8‴), MeO−C(9‴)	H−C(7‴), H−C(8‴), MeO−C(9‴)		H−C(7‴), H−C(8‴), MeO−C(9‴)	

except that almost all signals appeared as two sets due to a nonsymmetrical structure of **2**. However, they showed only five MeO signals instead of the six of **1**, suggesting that helicterin B could be a demethylated derivative of **1**.

The planar structure of **2** was elucidated on the basis of the HMBC spectrum (*Table 3*). The position of the demethylation was determined to be C(I-3′) based on the long-range correlations in the HMBC spectrum (long-range correlations of MeO protons with the ketal atom C(II-3′) and the ester CO atoms C(I-9″), C(I-9‴), C(II-9″), and C(II-9‴)). The connectivity of the two neolignan units was determined to be of type **A** (see *Fig.*) from the long-range correlations H−C(II-4′)/C(I-3′) and H−C(I-4′)/C(II-3′). The relative configuration of **2**, except for that at the (3,4-dihydroxyphenyl)lactic acid moieties, was determined by a series of difference NOE experiments.

NOE Enhancements observed from H−C(I-6′) to H−C(I-7) and from H−C(II-6′) to H−C(II-7) indicated that H−C(7) in both units should have β orientation. On the other hand, NOEs from H−C(I-2), H−C(I-4′), and MeO−C(I-3′) to H−C(I-8) revealed that H−C(I-4′), H−C(I-8′), and the 3,4-dihydroxyphenyl group at C(I-7′) should have α orientation, while the same configuration in unit II was elucidated based on the NOEs from H−C(II-2) to H−C(II-8) and H−C(II-4′) and from H−C(II-4′) to H−C(II-2) and H−C(II-8). Moreover, the NOE enhancement observed between H−C(I-4′) and H−C(II-4′) supported the type-**A** connectivity of the two monomer units.

Helicterins C (**3**) *and D* (**4**). The molecular formulas of **3** and **4** were determined as $C_{69}H_{68}O_{28}$ by high-resolution FAB-MS. Their UV and IR spectra were similar, resembled those of **1** and **2**, and showed the absorptions of phenyl, OH, and ester CO groups. Their ^{1}H- and ^{13}C-NMR spectra were also similar and resembled those of **1** (*Tables 1* and *2*), except for the lack of the signals due to a methyl 3-(3,4-dihydroxyphenyl)lactate moiety and the presence of an additional MeO signal. These data and a comparison of their compositions with that of **1** indicated that **3** and **4** should have a MeO group instead of the methyl 3-(3,4-dihydroxyphenyl)lactate moiety found in **1**. To ascertain the locations of the additional MeO groups and to determine the structures of **3** and **4**, COSY, HETCOR, and HMBC experiments were performed. In the HMBC spectrum of **3** (*Table 3*), the protons of the additional MeO group showed the long-range correlation with C(II-9), while in the HMBC spectrum of **4**, the correlation was observed with C(II-9′). These correlations were consistent with the replacement of the methyl 3-(3,4-dihydroxyphenyl)lactate moiety at C(II-9) by a MeO group in **3**, and of that at C(II-9′) by a MeO group in **4**.

Helicterins E (**5**) *and F* (**6**). The molecular formulas of **5** and **6** were determined to be $C_{68}H_{66}O_{28}$ by high-resolution FAB-MS. Their UV and IR spectra were also similar to those of **1**–**4** and showed the absorptions of phenyl, OH, and ester CO groups. Their ^{1}H- and ^{13}C-NMR spectra resembled each other and those of **2** (*Tables 1* and *2*), except for the lack of the signals due to a methyl 3-(3,4-dihydroxyphenyl)lactate moiety and the presence of an additional MeO signal. These data and a comparison of their compositions with that of **2** indicated that **5** and **6** should have a MeO group instead of a methyl 3-(3,4-dihydroxyphenyl)lactate moiety in **2**. The structures of **5** and **6** were determined by the analyses of the COSY, HETCOR, and HMBC data, establishing for **5** the replacement of the methyl 3-(3,4-dihydroxyphenyl)lactate moiety at C(II-9) of **2** by this MeO group, and for **6** the presence of the methyl 3-(3,4-dihydroxyphenyl)lactate moiety at C(II-9) and of a MeO group at C(I-3′).

Among the seven ester CO C-atoms of **5**, three showed a three-bond long-range correlation with the methine proton of the corresponding methyl 3-(3,4-dihydroxyphenyl)lactate moiety (C(I-9)/H–C(I-8″), C(I-9′)/H–C(I-8‴), C(II-9′)/H–C(II-8‴)), while the other four (C(I-9″), C(I-9‴), C(II-9), C(II-9‴)) revealed that with the MeO protons (*Table 3*). Moreover, only one (C(II-3′)) of two ketal C-atoms showed the correlations with the protons of a MeO group.

As in the case of **5**, the HMBC spectrum of **6** showed three-bond long-range correlations of three ester CO C-atoms with the methine proton of the corresponding methyl 3-(3,4-dihydroxyphenyl)lactate moiety (C(I-9)/H–C(I-8″), C(I-9′)/H–C(I-8‴), C(II-9)/H–C(II-8″)) and those of four ester CO C-atoms (C(I-9″), C(I-9‴), C(II-9′), C(II-9″)) with the MeO protons (*Table 3*). Of the long-range correlations of the ketal C-atoms, however, that of unit I was correlated with the protons of a MeO group.

3. Phytochemistry. – The six new compounds, helicterins A–F (**1**–**6**), belong to the class of the neolignans1) and are dimers of (7.5′,8.2′)-neolignans with a bicyclo[2.2.2]octene C-framework. Previously, sterols, triterpenoids, and flavonoids were reported as constituents of *H. isora* [10]. In the previous paper [9], we reported helisterculins A (**7**) and B (**8**), two (7.5′,8.2′)-neolignans with the bicyclo[2.2.2]octene C-framework, and helisorin (**9**), a (2.8′,4.6′,5.7′)-neolignan with a very rare 3.9-methano-3*H*-fluorene C-framework as the first example of neolignans of *H. isora*, and recently three new rosmarinic acid derivatives have also been reported together with rosmarinic acid itself [11]. Although many neolignans have been reported [12], only two, yunnaneic acids A and B from *Salvia yunnanensis* (Labiatae), belong to the dimeric (7.5′,8.2′)-neolignans with the bicyclo[2.2.2]octene C-framework [13]. Thus, helicterins A–F (**1**–**6**) are the first example of the dimeric (7.5′,8.2′)-neolignans from *H. isora.*

4. Biogenetic Consideration. – The structures of **1**–**6** suggest two probable biogenetic pathways, *i.e.*, a radical-coupling pathway recognized as a biosynthetic route for lignans and neolignans [12] and a *Diels-Alder* reaction pathway suggested for neolignans containing the bicyclo[2.2.2]octene structure [13][14] (see *Scheme*). As noted previously [9], however, the radical-coupling pathway seems more reasonable. The coupled product, a dioxo derivative, could be reduced to produce **7**, **8**, and also a plausible hydroxy-oxo intermediate that would dimerize to produce the helicterins (*Scheme*).

5. Reverse Transcriptase Inhibitory Activity. – The inhibitory activity of helicterins A–F (**1**–**6**) against AMV-RT was examined by means of [*methyl*-^{3}H]thymidine 5′-triphosphate (d[*methyl*-^{3}H]TTP) or 2′-deoxy[8-^{3}H]guanosine 5′-triphosphate (d[8-^{3}H]GTP) as a template primer [4]. The inhibitory activities of **1**–**6** were mild to weak (IC_{50}: **1**, 66 µM; **2**, 172 µM; **3**, 417 µM; **4**, 372 µM; **5**, 120 µM; **6**, 226 µM). But it should be noted here that the inhibitory activity of **1** was equal to that of a positive control adriamycin (IC_{50}: 66 µM).

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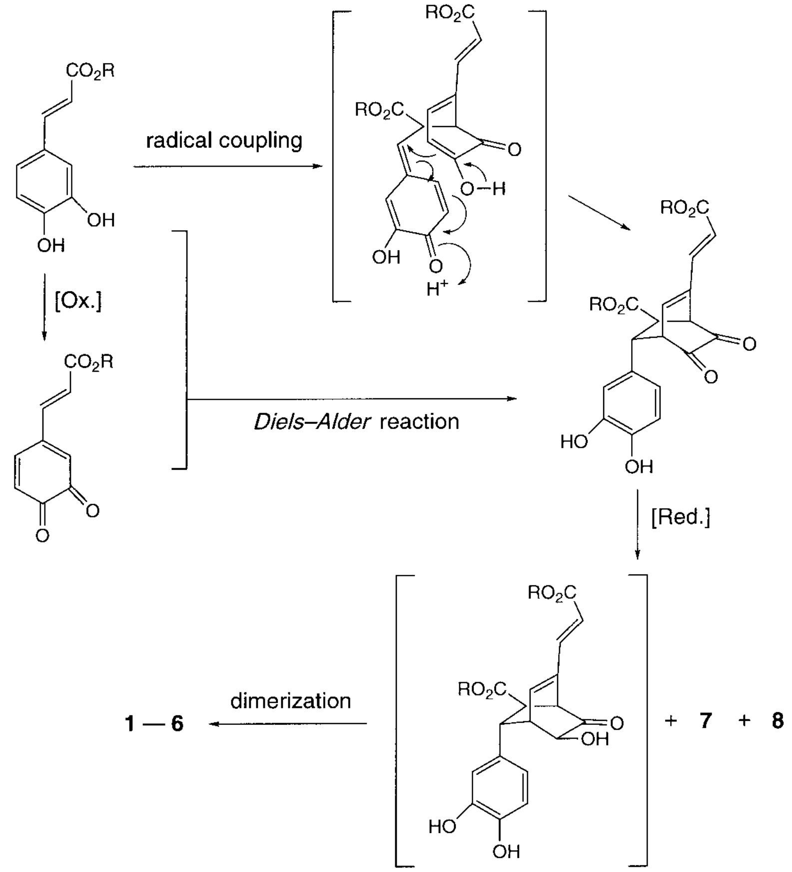
Experimental Part

General. Prep. TLC: *Merck* precoated silica gel $60F_{254}$ plate (0.5-mm thick); 20% MeOH/$CHCl_3$. Prep. HPLC: *Japan-Analytical-Industry-LC-908* system; *ODS-80TM*™ column (215 × 300 mm; *Toso*); mobile phase: 35% MeCN/1M AcOH. $[\alpha]_D^{26}$: *Jasco-DIP-140* digital polarimeter; *c* in g sample/100 ml solvent. UV Spectra:

Scheme. *Probable Biogenetic Pathways for the New Neolignans* **1**–**6**



Shimadzu-UV-160A spectrophotometer; λ_{max} (log ε) in nm. IR Spectra: *Jasco-IRA-2* spectrophotometer; $\tilde{\nu}_{max}$ in cm^{-1}. NMR Spectra: *Jeol-JNM-GX400* (400 (^1H) and 100 MHz (^{13}C)) instrument; CD_3OD solns. with $SiMe_4$ as an internal standard; δ in ppm, *J* in Hz. FAB-MS and HR-FAB-MS: *Jeol-JMS-SX102* mass spectrometer with glycerol as matrix.

Reverse Transcriptase Inhibitory Activity. Inhibitory activities of extracts, fractions, and compounds against AMV-RT were examined by the literature method [4], with d[*methyl*-^3H]TTP or d[8-^3H]GTP as a template primer.

Isolation. The H_2O extract of the powdered dried fruits of *H. isora* (2.5 kg), purchased in 1991 in Java, Indonesia, was fractionated into an AcOEt-soluble fraction (*A*, 2.4 g), a BuOH-soluble fraction (*B*, 5.8 g), and a H_2O-soluble fraction (*C*, 210 g). A portion of *Fr. C* (160 g) was treated with ion-exchange resin *Amberlite IR-120B* (H^+ form, 400 g; *Organo*) and then separated into a MeOH-soluble fraction (*D*[2]), 95 g) and a MeOH-insoluble fraction (*E*, 40 g). Fr. *D* (80 g) was chromatographed on a *Diaion-HP-20P* column (8.3 × 22 cm) with 0–70% MeOH/H_2O to give five fractions: *D.1* (H_2O eluate, 17.6 g), *D.2* (20% MeOH/H_2O eluate, 5 g), *D.3* (40% MeOH/H_2O eluate, 4.5 g), *D.4* (70% MeOH/H_2O eluate, 12.6 g) and *D.5* (MeOH eluate, 15.8 g) [9].

Fr. D.5 (15.8 g) was separated by a *Sephadex-LH-20* column (5.2 × 48 cm) with 40–100% MeOH/H_2O to give ten fractions: *Fr. D.5.1* (40% MeOH/H_2O eluate, 0.64 g), *Fr. D.5.2* (50% MeOH/H_2O eluate, 0.67 g), *Fr.*

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[2]) In the previous paper [9], the MeOH-soluble and MeOH-insoluble fractions were mislabeled; *i.e.*, the MeOH-soluble fraction was fraction *E* and the MeOH-insoluble fraction was fraction *D*.

D.5.3 (60% MeOH/H_2O eluate, 2.3 g), *Fr. D.5.4* (60% MeOH/H_2O eluate, 1.3 g), *Fr. D.5.5* (60% MeOH/H_2O eluate, 1.7 g), *Fr. D.5.6* (60% MeOH/H_2O eluate, 0.54 g), *Fr. D.5.7* (60% MeOH/H_2O eluate, 1.5 g), *Fr. D.5.8* (70% MeOH/H_2O eluate, 3.0 g), *Fr. D.5.9* (80% MeOH/H_2O eluate, 2.3 g), *Fr. D.5.10* (90 and 100% MeOH/H_2O eluates, 0.26 g). *Fr. D.5.4* was subjected to prep. HPLC to afford three fractions having t_R 114, 132, and 142 min; these gave, after prep. TLC (20% MeOH/$CHCl_3$), helicterins F (**6**; 14.8 mg), C (**3**; 18.0 mg), and D (**4**; 19.3 mg), resp. *Fr. D.5.5* was also subjected to prep. HPLC and the fractions having t_R 92, 104, and 142 min to prep. TLC (20% MeOH/$CHCl_3$), to give helicterins E (**5**; 17.1 mg), B (**2**; 40.3 mg), and A (**1**; 37.3 mg), resp.

Helicterin A (*=12,14-(3,4-Dihydroxyphenyl)-3,8-bis{3-{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethoxy}-3-oxoprop-1-enyl}-1,4,4a,5a,6,9,9a,10a-octahydro-4a,9a-dimethoxy-1,4:6,9-diethanodibenzo[*b,e*][1,4]dioxin-11,13-dicarboxylic Acid Bis{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethyl}Ester*; **1**). Colorless amorphous solid. $[\alpha]_D^{26} = +2.1$ ($c = 0.40$, MeOH). UV (MeOH): 281 (4.29). IR (KBr): 3418, 1735, 1630, 1521, 1441. ^1H- and ^{13}C-NMR (CD_3OD): *Tables 1* and *2*. FAB-MS: 1523 ($[M-H]^-$). HR-FAB-MS: 1523.4221 ($C_{78}H_{75}O_{32}^-$; calc. 1523.4241).

Helicterin B (*=12,14-(3,4-Dihydroxyphenyl)-3,8-bis{3-{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethoxy}-3-oxoprop-1-enyl}-1,4,4a,5a,6,9,9a,10a-octahydro-4a-hydroxy-9a-methoxy-1,4:6,9-diethanodibenzo[*b,e*][1,4]dioxin-11,13-dicarboxylic Acid Bis{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethyl} Ester*; **2**). Colorless amorphous solid. $[\alpha]_D^{26} = +4.2$ ($c = 0.40$, MeOH). UV (MeOH): 280 (4.59). IR (KBr): 3415, 1736, 1629, 1522, 1444, 1367. ^1H- and ^{13}C-NMR (CD_3OD): *Tables 1* and *2*. FAB-MS: 1509 ($[M-H]^-$). HR-FAB-MS: 1509.4104 ($C_{77}H_{73}O_{32}^-$; calc. 1509.4085).

Helicterin C (*=12,14-(3,4-Dihydroxyphenyl)-3,8-bis{3-{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethoxy}-3-oxoprop-1-enyl}-1,4,4a,5a,6,9,9a,10a-octahydro-4a,9a-dimethoxy-1,4:6,9-diethanodibenzo[*b,e*][1,4]dioxin-11,13-dicarboxylic Acid 11-{1-[(3,4-Dihydroxyphenyl)methyl]-2-methoxy-2-oxoethyl} 13-Methyl Ester*; **3**). Colorless amorphous solid. $[\alpha]_D^{26} = -10.0$ ($c = 0.32$, MeOH). UV (MeOH): 280 (4.65). IR (KBr): 3436, 1723,1630, 1522, 1442, 1364. ^1H- and ^{13}C-NMR (CD_3OD): *Tables 1* and *2*. FAB-MS: 1343 ($[M-H]^-$). HR-FAB-MS: 1343.3807 ($C_{69}H_{67}O_{28}^-$; calc. 1343.3819).

Helicterin D (*=12,14-(3,4-Dihydroxyphenyl)-3-{3-{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethoxy}-3-oxoprop-1-enyl}-1,4,4a,5a,6,9,9a,10a-octahydro-4a,9a-dimethoxy-8-(3-methoxy-3-oxoprop-1-enyl)-1,4:6.9-diethanodibenzo[*b,e*][1,4]dioxin-11,13-dicarboxylic Acid Bis{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethyl} Ester*; **4**). Colorless amorphous solid. $[\alpha]_D^{26} = +0.3$ ($c = 0.87$, MeOH). UV (MeOH): 279 (4.66). IR (KBr): 3432, 1737, 1630, 1607, 1522, 1441, 1366. ^1H- and ^{13}C-NMR (CD_3OD): *Tables 1* and *2*. FAB-MS: 1345 ($[M-H]^-$). HR-FAB-MS: 1343.3822 ($C_{69}H_{67}O_{28}^-$; calc. 1343.3819).

Helicterin E (*=12,14-(3,4-Dihydroxyphenyl)-3,8-bis{3-{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethoxy}-3-oxoprop-1-enyl}-1,4,4a,5a,6,9,9a,10a-octahydro-4a-hydroxy-9a-methoxy-1,4:6.9-diethanodibenzo-[*b,e*][1,4]dioxin-11,13-dicarboxylic Acid 13-{1-[(3,4-Dihydroxyphenyl)methyl]-2-methoxy-2-oxoethyl} 11-Methyl Ester*; **5**). Colorless amorphous solid. $[\alpha]_D^{26} = +17.0$ ($c = 0.74$, MeOH). UV (MeOH): 278 (4.71). IR (KBr): 3396, 1736, 1630, 1527, 1441, 1364. ^1H- and ^{13}C-NMR (CD_3OD): *Tables 1* and *2*. FAB-MS: 1329 ($[M-H]^-$). HR-FAB-MS: 1329.3625 ($C_{68}H_{65}O_{28}^-$; calc. 1329.3662).

Helicterin F (*=12,14-(3,4-Dihydroxyphenyl)-3-{3-{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethoxy}-3-oxoprop-1-enyl}-1,4,4a,5a,6,9,9a,10a-octahydro-4a-methoxy-9a-hydroxy-8-(3-methoxy-3-oxoprop-1-enyl)-1,4:6,9-diethanodibenzo[*b,e*][1,4]dioxin-11,13-dicarboxylic Acid Bis{1-[(3,4-dihydroxyphenyl)methyl]-2-methoxy-2-oxoethyl} Ester*; **6**). Colorless amorphous solid. $[\alpha]_D^{26} = +7.4$ ($c = 0.86$, MeOH). UV (MeOH): 280 (4.50). IR (KBr): 3392, 1732, 1628, 1520, 1447, 1362. ^1H- and ^{13}C-NMR (CD_3OD): *Tables 1* and *2*. FAB-MS: 1329 ($[M-H]^-$). HR-FAB-MS: 1329.3698 ($C_{68}H_{65}O_{28}^-$; calc. 1329.3662).

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